Renal stone epidemiology in Rochester, Minnesota: An update

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Studies in Western countries have suggested an increasing incidence of nephrolithiasis (NL) in the latter part of the 20th century. Therefore, we updated NL epidemiology data for the Rochester population over the years 1970–2000. All Rochester residents with any diagnostic code that could be linked to NL in the years of 1970, 1980, 1990, and 2000 were identified, and the records reviewed to determine if they met the criteria for a symptomatic kidney stone as defined in a previous Rochester, MN study. Age-adjusted incidence (±s.e.) of new onset symptomatic stone disease for men was 155.1 (±28.5) and 105.0 (±16.8) per 100 000 per year in 1970 and 2000, respectively. For women, the corresponding rates were 43.2 (±14.0) and 68.4 (±12.3) per 100 000 per year, respectively. On average, rates for women increased by about 1.9% per year ($P = 0.064$), whereas rates for men declined by 1.7% per year ($P = 0.019$). The overall man to woman ratio decreased from 3.1 to 1.3 during the 30 years ($P = 0.006$). Incident stone rates were highest for men aged 60–69 years, whereas for women, they plateaued after age 30. Therefore, since 1970 overall NL incidence rates in Rochester have remained relatively flat. However, NL rates for men have declined, whereas rates for women appear to be increasing. The reasons remain to be determined.

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Nephrolithiasis (NL) is a common disorder responsible for substantial human suffering and economic cost to society. Renal stones have long been associated with affluence,[1] and dietary factors associated with higher socioeconomic status have been implicated.[2] Studies over the last half century, including recently,[3,4] suggest that the incidence has been steadily increasing, presumably related to diet and lifestyle changes. In 1979, researchers at Mayo Clinic carefully examined the epidemiology of kidney stone disease in Rochester, MN, USA.[5] Between 1950 and 1974, 672 incident cases of symptomatic NL were identified. A trend for a steadily increasing rate of incident stones over the study period was apparent, particularly in men, in this seminal report describing NL epidemiology in a community-based cohort. We now report an update of the incidence of symptomatic renal stones in Rochester, MN to determine if these trends persist.

RESULTS

There were 41, 58, 78, and 71 cases that met our criteria for incident symptomatic stones in 1970, 1980, 1990, and 2000, respectively (Table 1). Radiographic confirmation was obtained in 177 cases (72% of the 248 incident cases). The mean age at incident stone event was 44.8 years in men and 40.9 years in women. Among the 248 incident cases, the overall man to woman ratio was 1.73; however, it decreased from 3.1 to 1.3 over the 30-year period (Figure 1). For reference, Figure 1 includes incidence rates from the previous Rochester, MN, USA study for calendar years 1950–1974,[5] demonstrating that incidence rates correlate in the time period of overlap (~1970). From 1970 to 2000, men experienced a significant average decline in incident stone rates of 1.7% per year (age-adjusted $P = 0.019$), whereas rates for women increased by 1.9% per year (age-adjusted $P = 0.064$), despite a slight decline from 1990 to 2000 (Table 1). Comparison of these trends between men and women was statistically significant ($P = 0.006$ for test of interaction between sex and calendar year).

In Figure 2, rates of incident stone events were averaged over the 4 years 1970, 1980, 1990, and 2000, and are shown for men and women by decade of age. Overall, incident stones were distinctly more common for men aged 60–69

Table 1 | Incident symptomatic stone rates in Rochester, MN, USA by decade

	Men		Women		Total	
Year	Rate (±s.e.)[a]	Cases	Rate (±s.e.)[a]	Cases	Rate (±s.e.)[b]	Cases
1970	155.1 (±28.5)	31	43.2 (±14.0)	10	98.7 (±15.7)	41
1980	183.7 (±29.3)	42	53.6 (±13.8)	16	116.5 (±15.8)	58
1990	144.0 (±22.3)	44	92.4 (±16.3)	34	117.1 (±13.6)	78
2000	105.0 (±16.8)	40	68.4 (±12.3)	31	85.1 (±10.2)	71
Total	140.6 (±11.4)	157	65.8 (±7.0)	91	101.8 (±6.6)	248

[a]Annual age-adjusted (to US 2000 census data) rate of new onset stone disease per 100 000 population.
[b]Annual age- and sex-adjusted (to US 2000 census data) rate of new onset stone disease per 100 000 population.

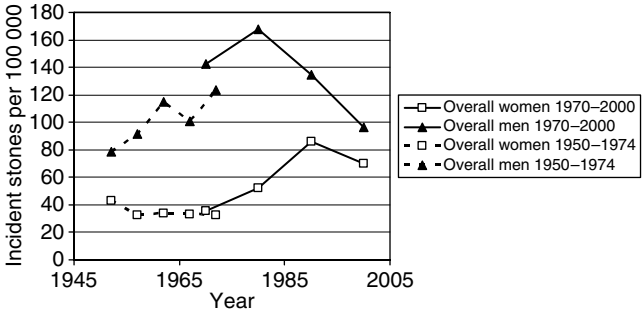

Figure 1 | Incident symptomatic stone rates 1950–2000. Solid lines depict data form the current Rochester, MN study (1970–2000). For comparison, the dotted lines indicate data from the previous Rochester, MN, USA study by Johnson *et al.* (1950–1974).[5] To facilitate comparison between the two studies, as in the earlier report, all rates are age adjusted to the 1960 US white population.

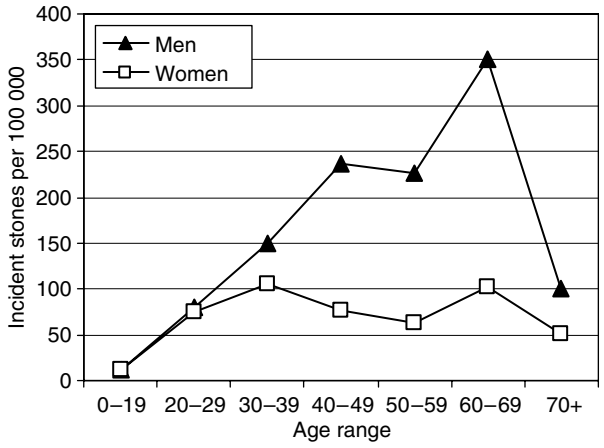

Figure 2 | Incident symptomatic stone rates by age group for men and women in Rochester, MN, USA between 1970 and 2000, averaged for the years 1970–2000.

years over this time period. Among women, incident stone rates were less overall, and roughly equivalent between ages 20 and 70 years, although slightly more common for those 30–39 and 60–69 years (Figure 2). When broken down by calendar year and age group, the decline in incident stone events for men was apparent for all age groups, except those over 70 years (Figure 3); however, only for the 20–29 years age group was the decline statistically significant ($P=0.028$). In women, rates appeared to generally increase across all age

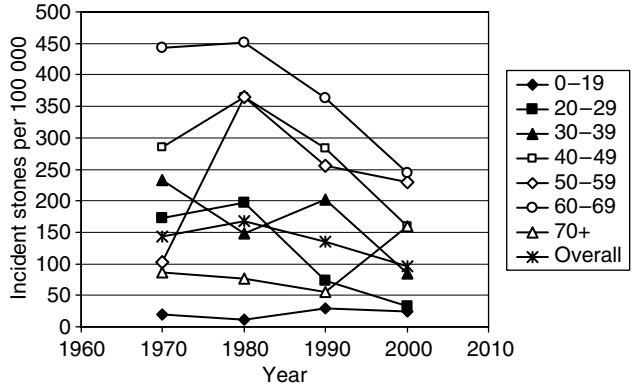

Figure 3 | Incident symptomatic stone rates in Rochester, MN, USA 1970–2000 for men by age group between the years 1970–2000.

groups (Figure 4), with those aged 20–29 years exhibiting a sevenfold rise between 1970 and 2000 ($P=0.014$); trends over time in other age groups did not reach statistical significance.

Primary stone type was known for 153 of 248 incident cases (62%), among which 74% (113) were calcium oxalate, 20% (31) calcium phosphate and 6% (9) uric acid. Men were somewhat more likely to have calcium oxalate stones than women (78 vs 67%, $P=0.10$ adjusted for age and year using logistic regression) and hence less likely to have calcium phosphate stones (15 vs 29%, $P=0.029$). Table 2 provides the distribution by type for each calendar year of study. There were no significant time trends in the proportion with each of the major stone types ($P=0.57$ calcium oxalate, $P=0.96$ for calcium phosphate, adjusting for age and gender). Owing to the large number of events for which type was unknown, it was not possible to estimate incidence rates for each stone type.

The rate for all symptomatic stone events (incident plus recurrent, men and women) appears to have remained relatively flat for both sexes over the years 1970–2000 ($P=0.33$ for trends over time, Table 3). Therefore, the overall health burden of symptomatic stone disease has remained constant over the past 30 years in Rochester.

DISCUSSION

Kidney stones are common, with some estimates suggesting they affect 12% of men and 5% of women in industrialized

countries by age 70,[6] which extrapolates to 900 000 persons in the United States each year.[7] Correspondingly, the economic impact in the United States was recently estimated in one study at $2.1 billion per year[8] to as much as $5.3 billion in another,[9] with the vast majority ($4.5 billion) attributed to direct medical costs. Even though newer techniques such as extracorporeal shock wave lithotripsy and percutaneous lithotomy can dislodge and remove even large stones, these procedures are expensive, and their longer-term renal consequences are unknown.[10–12] Therefore, accurate information about stone incidence rates has obvious health and economic implications.

Recent reports suggest a continuing upward trend in stone rates. For example, between 1979 and 2000, the incidence increased nearly threefold in Germany (0.54–1.47%), with a resulting rise in prevalence from 4.0 to 4.7% among the population as a whole. Among German men aged 50–64 years, the prevalence was even higher at 9.7%, and over 40% of the stone formers were recurrent.[3] Recently, in the United States the prevalence of renal stones was noted to increase in both men (4.9–6.3%) and women (2.8–4.1%) between the 2nd (1976–1980) and 3rd (1988–1994) National Health and Nutrition Examination Surveys.[4] Importantly, in both the German and American studies, stone rates were determined by self-reported survey of healthier and younger volunteer participants as compared to our study, which obtained rates for all members of a geographically defined population. Differences in subject selection (volunteers vs all residents), event rates (incidence vs prevalence), and case identification (self-report vs medical record review) make comparison of time trends across studies difficult.

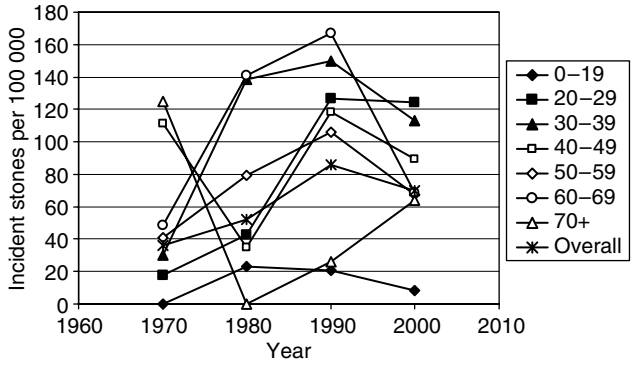

Figure 4 | Incident symptomatic stone rates in Rochester, MN, USA 1970–2000 for women by age group between the years 1970–2000.

Table 2 | Incident symptomatic stone types in Rochester, MN, USA by decade

	Year of diagnosis			
	1970	1980	1990	2000
Total stones	41	58	78	71
Stone type known: number (% of total)	18 (44)	32 (55)	41 (53)	62 (87)
% Calcium Oxalate	72.2	78.1	70.7	74.2
% Calcium Phosphate	22.2	12.5	29.3	17.7
% Uric Acid	5.6	9.4	0	8.1

Values are the percent of a given stone type among those incident cases with analyses available. Stones were classified based upon the major (>50%) component.

The previous Rochester, MN, USA study demonstrated an upward trend of stone incidence rates between the years of 1950 and 1974, particularly in men.[5] Using the same criteria to identify symptomatic stone events, our study suggests that these dynamics may now be changing. Incidence rates for men continued to rise through 1980, but appear to have fallen since. In contrast, for women the incidence rates continued to rise through at least 1990, although they may have declined over the last decade. A dramatic increase among those aged 20–29 years appears to account for the increase of stone events in women. Overall, for incident symptomatic stones, the man to woman ratio of 3.2 in 1970 fell to 1.3 in 2000 (Figure 1), although the total rates for both sexes, including both incident and recurrent symptomatic stones, have remained relatively flat for the past 30 years (Table 3).

By design we included only symptomatic stones, so that our present rates would be comparable to those previously reported for this population[5] and provide a direct indication of any changes in stone occurrence rates. It is possible that increasing utilization of high-resolution imaging technology, especially computed tomography scanning, could increase the detection of incidental (asymptomatic) stone rates. Diagnosis of these asymptomatic stones could potentially result in additional stone removal procedures, dietary advice or possibly even medications, any of which could potentially decrease stone growth and/or future symptomatic stone episodes.

Table 3 | Total (incident and recurrent) symptomatic stone rates in Rochester, MN, USA by decade

	Men		Women		Total	
Year	Rate (±s.e.)[a]	Cases	Rate (±s.e.)[a]	Cases	Rate (±s.e.)[b]	Cases
1970	189.0 (±31.8)	37	47.8 (±4.8)	11	116.8 (±17.1)	48
1980	229.7 (±32.8)	52	59.4 (±14.2)	19	142.2 (±17.5)	71
1990	171.6 (±24.2)	53	107.2 (±17.4)	40	138.1 (±14.7)	93
2000	125.9 (±18.4)	48	77.7 (±13.2)	35	100.1 (±11.0)	83
Total	170.1 (±12.5)	190	75.4 (±7.5)	105	121.0 (±7.2)	295

[a]Annual age-adjusted (to US 2000 census data) rate of new onset stone disease per 100 000 population.
[b]Annual age- and sex-adjusted (to US 2000 census data) rate of new onset stone disease per 100 000 population.

Alternatively, the epidemiology of stone disease could have changed over the past 20 years. If so, one might speculate that important dietary or lifestyle changes could be responsible, as these are known to influence stone formation rates.[13–21] For example, among women low dietary calcium intake correlates with increased stone risk,[14] although the underlying mechanisms are not clear.[22] Nevertheless, declining consumption of calcium-rich dairy products among younger women, as has been documented in certain populations,[23] is one potential factor that could contribute to the increasing incident stone rates we observed among this group (Figure 4).

In summary, our data suggest that, in Rochester over the past 20 years, rates of incident symptomatic stones have fallen in men, but increased in women. Explanations remain to be investigated, but could involve utilization of imaging technology or changes in diet and lifestyle.

MATERIALS AND METHODS

Study setting: Rochester Epidemiology Project

Olmsted County, MN, USA (2000 census population, 124 277) and its central city Rochester (2000 census population, 85 806) are located in the southeastern part of the State, approximately 128 km from the nearest major metropolitan area. Population-based epidemiologic research in Olmsted County is facilitated by its relative geographic isolation. Nearly all of the medical care delivered to Olmsted County residents is provided by either the Mayo Clinic or the Olmsted Medical Center and their respective affiliated hospitals.[24] Since 1907, every Mayo Clinic patient has been assigned a unique identifier, and all information from every contact is contained within a single dossier (including office, emergency department, and nursing home visits and hospital in-patient or outpatient admissions). This detailed information includes a medical history, clinical assessments, consultation reports, dismissal summaries, laboratory and radiology results, and correspondence. The diagnoses assigned at each visit are coded and entered into continuously updated computer files. These files constitute the Rochester Epidemiology Project diagnostic index. With funding from the National Institutes of Health (Grant AR 30582), the diagnostic index and record linkage was expanded to include the other providers of medical care to local residents, including the Olmsted Medical Center and the few private practitioners in the area. Thus, the details of almost all of the medical care provided to the residents of Rochester are available for study.[24]

Sample description

This study was approved by the Mayo Clinic and Olmsted Medical Center Institutional Review Boards. Rochester Epidemiology Project resources were used to identify all Rochester residents with any Mayo diagnostic code that could possibly be linked to NL in the years of 1970 ($n=68$), 1980 ($n=91$), 1990 ($n=107$) and 2000 ($n=107$) (Mayo diagnostic index codes 5920, 5921, 5940, 5949, 14675, 15672, 15673, and 15674; equivalent ICD-9-CM codes[25] 592, 594 and 275.11). In accordance with Minnesota state law,[24] three patients who did not grant access to their records for research were deleted from further review. As defined in detail in the previous study,[5] the provider-linked detailed medical records of the remaining potential cases ($n=370$) were reviewed to determine if they met the criteria for a symptomatic kidney stone event while a resident of Rochester, and whether the event was incident or recurrent. Kidney stone passage was classified as confirmed if the patient presented with a characteristic pattern of flank pain of sudden onset with radiation to the groin (renal colic). If the pain was atypical, additional evidence, either hematuria or radiographic confirmation, was required. Persons who had asymptomatic stones (e.g., detected incidentally on an imaging study), simple bladder stones or those who manifested other primary problems that might have secondarily caused the stones (e.g., ureteral reflux with urinary tract infection, fat malabsorption or cystinuria) were excluded.[5] Age, sex and, if available, stone type were noted.

Of the 370 potential cases, 344 met the criteria for confirmed symptomatic stone events while a Rochester resident. The reasons for exclusion were as follows: three were non-Rochester residents at the time of stone diagnosis, 19 did not meet the pre-established criteria for a symptomatic stone event, two did not have sufficient material in the medical record for determination and two had evidence of infection-mediated disease (struvite stones). Of the 344 confirmed kidney stone events, 248 were incident and 96 were recurrent.

Statistical analysis

Age group (<20, 20–29, 30–39, 40–49, 50–59, 60–69 and 70+ years) and gender-specific incidence rates for each calendar year (1970, 1980, 1990 and 2000) were calculated by dividing the number of cases by the estimated Rochester population in that year as determined by the US decennial census. Poisson regression was used to assess gender and age effects and to test for time trends in incidence using the 56 data points determined by all combinations of calendar year, gender and age group. Adjusted incidence rates and s.e. were calculated using the direct method and the sex and age distribution of the US 2000 total population, except in Figure 1, where the 1960 US white population was used instead in order to allow comparison with our earlier study.[5]

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